



COL1A2 gene

collagen type I alpha 2 chain

Normal Function

The *COL1A2* gene provides instructions for making part of a large molecule called type I collagen. Collagens are a family of proteins that strengthen and support many tissues in the body, including cartilage, bone, tendon, skin, and the white part of the eye (the sclera). Type I collagen is the most abundant form of collagen in the human body.

A component of type I collagen called the pro- $\alpha 2(I)$ chain is produced from the *COL1A2* gene. Collagens begin as rope-like procollagen molecules that are each made up of three chains. Type I collagen is composed of two pro- $\alpha 1(I)$ chains (which are produced from the *COL1A1* gene) and one pro- $\alpha 2(I)$ chain.

The triple-stranded procollagen molecules are processed by enzymes outside the cell to create mature collagen. The collagen molecules then arrange themselves into long, thin fibrils that form stable interactions (cross-links) with one another in the spaces between cells. The cross-links result in the formation of very strong type I collagen fibers.

Health Conditions Related to Genetic Changes

Ehlers-Danlos syndrome

Several mutations in the *COL1A2* gene can cause a form of Ehlers-Danlos syndrome known as the arthrochalasia type. Ehlers-Danlos syndrome is a group of disorders that affect the connective tissues that support the skin, bones, blood vessels, and many other organs and tissues. The arthrochalasia type is characterized by an unusually large range of joint movement (hypermobility) and dislocations of both hips at birth. The genetic changes, which affect one copy of the *COL1A2* gene in each cell, lead to the production of a pro- $\alpha 2(I)$ chain that is missing a critical segment. The absence of this segment interferes with the assembly and processing of pro- $\alpha 2(I)$ chains into mature type I collagen molecules. These changes mainly affect tissues that are rich in type I collagen, such as the skin, bones, and tendons.

Rarely, mutations in both copies of the *COL1A2* gene in each cell have been reported in people with a form of Ehlers-Danlos syndrome described as the cardiac valvular type. This rare condition is characterized by abnormalities of the valves in the heart, highly stretchy (elastic) skin, and joint hypermobility. The mutations that cause this form of the disorder prevent cells from producing any normal pro- $\alpha 2(I)$ chains. As

a result, type I collagen fibrils in the skin and other tissues cannot be assembled correctly. The abnormal collagen weakens connective tissues, which causes the signs and symptoms of this condition.

osteogenesis imperfecta

Mutations in the *COL1A2* gene occasionally cause osteogenesis imperfecta type I, the mildest form of this disorder. Most *COL1A2* mutations, however, cause more severe forms of osteogenesis imperfecta, including types II, III, and IV. People with this condition have bones that break easily, often from mild trauma or with no apparent cause.

Some *COL1A2* mutations delete pieces of the gene, which leads to a pro- $\alpha 2(I)$ chain that is missing critical regions. Other genetic changes alter the sequence of protein building blocks (amino acids) in the pro- $\alpha 2(I)$ chain, usually replacing the amino acid glycine with a different amino acid. In some cases, amino acid substitutions alter one end of the protein chain (called the C-terminus), which interferes with the assembly of collagen molecules. These *COL1A2* mutations prevent the normal production of type I collagen. When abnormal collagen is incorporated into developing bones and other connective tissues, it causes the serious medical problems associated with severe forms of osteogenesis imperfecta.

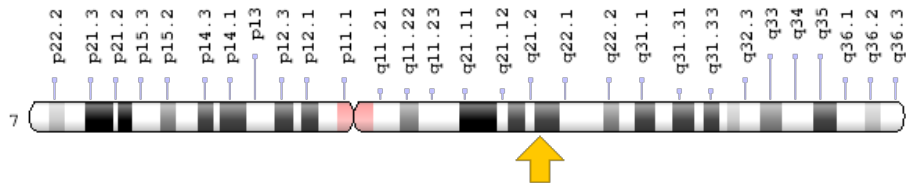
other disorders

People with certain *COL1A2* mutations exhibit the signs and symptoms of both osteogenesis imperfecta and Ehlers-Danlos syndrome (described above). These mutations include duplications of a large part of the gene, deletions of an important segment of the pro- $\alpha 2(I)$ chain, and genetic changes that result in an abnormally shortened version of the pro- $\alpha 2(I)$ chain. Mutations in the *COL1A2* gene alter the structure of type I collagen fibrils, which weakens connective tissue and leads to the characteristic features of these two conditions.

Chromosomal Location

Cytogenetic Location: 7q21.3, which is the long (q) arm of chromosome 7 at position 21.3

Molecular Location: base pairs 94,394,561 to 94,431,232 on chromosome 7 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- alpha 2 collagen type I
- CO1A2_HUMAN
- collagen I, alpha-2 polypeptide
- collagen of skin, tendon and bone, alpha-2 chain
- collagen type I alpha 2
- collagen, type I, alpha 2

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): Collagens Are the Major Proteins of the Extracellular Matrix
<https://www.ncbi.nlm.nih.gov/books/NBK26810/#A3551>
- Molecular Cell Biology (fourth edition, 2000): Collagen: The Fibrous Proteins of the Matrix
<https://www.ncbi.nlm.nih.gov/books/NBK21582/>
- The Cell: A Molecular Approach (second edition, 2000): Collagen Fibrils (figure)
<https://www.ncbi.nlm.nih.gov/books/NBK9874/?rendertype=figure&id=A2050>

GeneReviews

- COL1A1/2-Related Osteogenesis Imperfecta
<https://www.ncbi.nlm.nih.gov/books/NBK1295>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28COL1A2%5BTIAB%5D%29+OR+%28alpha+2+collagen+type+I%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5BIa%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D>

OMIM

- COLLAGEN, TYPE I, ALPHA-2
<http://omim.org/entry/120160>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
<http://atlasgeneticsoncology.org/Genes/COL1A2ID411ch7q22.html>
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=COL1A2%5Bgene%5D>
- Database Of Human Type I And Type III Collagen Mutations
<http://www.le.ac.uk/genetics/collagen/>
- HGNC Gene Family: Collagens
<http://www.genenames.org/cgi-bin/genefamilies/set/490>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=2198
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/1278>
- UniProt
<http://www.uniprot.org/uniprot/P08123>

Sources for This Summary

- Byers PH, Pyott SM. Recessively inherited forms of osteogenesis imperfecta. *Annu Rev Genet.* 2012;46:475-97. doi: 10.1146/annurev-genet-110711-155608. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23145505>
- Giunta C, Steinmann B. Gene symbol: COL1A2. Disease: Ehlers-Danlos syndrome type VIIIB. *Hum Genet.* 2008 Jun;123(5):540.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20960610>
- Malfait F, Symoens S, Coucke P, Nunes L, De Almeida S, De Paepe A. Total absence of the alpha2(I) chain of collagen type I causes a rare form of Ehlers-Danlos syndrome with hypermobility and propensity to cardiac valvular problems. *J Med Genet.* 2006 Jul;43(7):e36.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16816023>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2564565/>

- Malfait F, Symoens S, Goemans N, Gyftodimou Y, Holmberg E, López-González V, Mortier G, Nampoothiri S, Petersen MB, De Paepe A. Helical mutations in type I collagen that affect the processing of the amino-propeptide result in an Osteogenesis Imperfecta/Ehlers-Danlos Syndrome overlap syndrome. *Orphanet J Rare Dis*. 2013 May 21;8:78. doi: 10.1186/1750-1172-8-78.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23692737>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3662563/>
- Schwarze U, Hata R, McKusick VA, Shinkai H, Hoyme HE, Pyeritz RE, Byers PH. Rare autosomal recessive cardiac valvular form of Ehlers-Danlos syndrome results from mutations in the COL1A2 gene that activate the nonsense-mediated RNA decay pathway. *Am J Hum Genet*. 2004 May;74(5):917-30. Epub 2004 Apr 9.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15077201>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1181985/>
- Van Dijk FS, Sillence DO. Osteogenesis imperfecta: clinical diagnosis, nomenclature and severity assessment. *Am J Med Genet A*. 2014 Jun;164A(6):1470-81. doi: 10.1002/ajmg.a.36545. Epub 2014 Apr 8. Review. Erratum in: *Am J Med Genet A*. 2015 May;167A(5):1178.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/24715559>
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